

CLAIMS

1. A method for the treatment or prevention of a disorder wherein said disorder is selected from the group consisting of multiple myeloma, liquid tumor, liver cancer, thymus disorder, T-cell mediated autoimmune disease, endocrinological disorder, ischemia, and neurodegenerative disorder in a mammal comprising administering to said mammal an amount of a human anti-IGF-IR antibody that is effective in treating said disorder.

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2. The method of claim 1 wherein said liquid tumor is selected from the group consisting of acute lymphocytic leukemia (ALL) and chronic myelogenous leukemia (CML); wherein said liver cancer is selected from the group consisting of hepatoma, hepatocellular carcinoma, cholangiocarcinoma, angiosarcomas, hemangiosarcomas, hepatoblastoma; wherein said thymus disorder is selected from the group consisting of thymoma and thyroiditis, wherein said T-cell mediated autoimmune disease is selected from the group consisting of Multiple Sclerosis, Rheumatoid Arthritis, Systemic Lupus Erythematosus (SLE), Grave's Disease, Hashimoto's Thyroiditis, Myasthenia Gravis, Auto-Immune Thyroiditis, Bechet's Disease, wherein said endocrinological disorder is selected from the group consisting of Type II Diabetes, hyperthyroidism, hypothyroidism, thyroiditis, hyperadrenocorticism, and hypoadrenocorticism; wherein said ischemia is post cardiac ischemia, and wherein said neurodegenerative disorder is Alzheimer's Disease.

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3. The method of claim 1 comprising administering to said mammal said antibody in combination with an agent selected from the group consisting of a corticosteroid, anti-emetic, cancer vaccine, analgesic, anti-vascular agent, and anti-proliferative agent.

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4. The method of claim 1 comprising administering said antibody in combination with an anti-emetic agent, wherein said agent is selected from the group consisting of ondansetron hydrochloride, granisetron hydrochloride, metoclopramide, domperidone, haloperidol, cyclizine, lorazepam, prochlorperazine, dexamethasone, levomepromazine, or tropisetron.

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5. The method of claim 1 comprising administering said antibody in combination with a vaccine, wherein said vaccine is selected from GM-CSF DNA and cell-based vaccines, dendritic cell vaccines, recombinant viral vaccines, heat shock protein (HSP) vaccines, allogeneic or autologous tumor vaccines.

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6. The method of claim 1 comprising administering said antibody in combination with an analgesic agent, wherein said agent is selected from the group consisting of ibuprofen, naproxen, choline magnesium trisalicylate, or oxycodone hydrochloride.
- 5 7. The method of claim 1 comprising administering said antibody in combination with an anti-vascular agent, wherein said agent is selected from the group consisting of bevacizumab, or rhuMAb-VEGF.
- 10 8. The method of claim 1 comprising administering said antibody in combination with an anti-proliferative agent, wherein said agent is selected from the group consisting of farnesyl protein transferase inhibitors, $\alpha\text{v}\beta 3$ inhibitors, $\alpha\text{v}\beta 5$ inhibitors, p53 inhibitors, and PDGFR inhibitors.
- 15 9. The method of claim 1 wherein the antibody that binds to IGF-IR has the following properties:
a binding affinity for human IGF-IR of K_d of 8×10^{-9} or less;
inhibition of binding between human IGF-IR and IGF-1 with an IC_{50} of less than 100 nM; and
comprises a heavy chain amino acid sequence comprising human FR1, FR2, and
20 FR3 amino acid sequences that correspond to those of the VH DP-35, VIV-4/4.35, VH DP-47, or VH DP-71 gene, or conservative substitutions or somatic mutations therein, wherein the FR sequences are linked with CDR1, CDR2, and CDR3 sequences, and wherein the antibody also comprises CDR regions in its light chain from the A27, A30, or O12 gene.
- 25 10. The method of claim 1 wherein said antibody competes for binding with IGF-IR with an antibody having heavy and light chain amino acid sequences of an antibody selected from the group consisting of 2.12.1, 2.13.2, 2.14.3, 4.9.2, 4.17.3, and 6.1.1.
- 30 11. The method of claim 1 wherein said antibody comprises a heavy chain comprising the amino acid sequences of CDR-1, CDR-2, and CDR-3, and a light chain comprising the amino acid sequences of CDR-1, CDR-2, and CDR-3, of an antibody selected from the group consisting of 2.12.1, 2.13.2, 2.14.3, 4.9.2, 4.17.3, and 6.1.1, or sequences having changes from said CDR sequences selected from the group consisting of conservative changes, wherein said conservative changes are selected from the group consisting of
35 replacement of nonpolar residues by other nonpolar residues, replacement of polar charged residues by other polar uncharged residues, replacement of polar charged residues by other polar charged residues, and substitution of structurally similar residues; and non-conservative

substitutions, wherein said non-conservative substitutions are selected from the group consisting of substitution of polar charged residue for polar uncharged residues and substitution of nonpolar residues for polar residues, additions and deletions.

5 12. The method of claim 11 wherein said antibody comprises a heavy chain comprising the amino acid sequences of CDR-1, CDR-2, and CDR-3, and a light chain comprising the amino acid sequences of CDR-1, CDR-2, and CDR-3, of an antibody selected from the group consisting of 2.12.1, 2.13.2, 2.14.3, 4.9.2, 4.17.3, and 6.1.1.

10 13. The method of claim 1 wherein said antibody is selected from the group consisting of an antibody comprising a heavy chain amino acid sequence derived from human gene DP-47 and a light chain amino acid sequence derived from human gene A30.

15 14. A pharmaceutical composition for the treatment or prevention of a disorder in a mammal comprising an amount of a human anti-IGF-IR antibody that is effective in treating said disorder and a pharmaceutically acceptable carrier, wherein said disorder is selected from the group consisting of multiple myeloma, liquid tumor, liver cancer, thymus disorder, T-cell mediated autoimmune disease, endocrinological disorder, ischemia, and neurodegenerative disorder.

20 15. The pharmaceutical composition of claim 14 further comprising an amount of anti-emetic, cancer vaccine, analgesic, anti-vascular agent, and anti-proliferative agent that, in combination with said antibody, is effective in treating said disorder.

25 16. Use of an amount of a human anti-IGF-IR antibody in the preparation of a composition for the treatment or prevention of a disorder in a mammal that is effective in treating said disorder, wherein said disorder is selected from the group consisting of multiple myeloma, liquid tumor, liver cancer, thymus disorder, T-cell mediated autoimmune disease, endocrinological disorder, ischemia, and neurodegenerative disorder.

30 17. A method for the treatment or prevention of aging in a mammal comprising administering to said mammal an amount of an anti-IGF-IR antibody that is effective in said treatment or prevention.